

CLAIMS

1. A method for treating or preventing cancer, comprising:
administering to a subject having or at risk of developing cancer an effective amount
5 to upregulate CD20 expression of a nucleic acid, and
an anti-CD20 antibody.
2. The method of claim 1, wherein the nucleic acid is an immunostimulatory CpG
nucleic acid having an unmethylated CpG motif.
- 10 3. The method of claim 1, wherein the nucleic acid is an immunostimulatory T-rich
nucleic acid.
4. The method of claim 1, wherein the nucleic acid is an immunostimulatory poly-G
nucleic acid.
- 15 5. The method of claim 1, wherein the nucleic acid is bacterial DNA.
6. The method of claim 1, wherein the nucleic acid is eukaryotic DNA.
- 20 7. The method of claim 1, wherein the cancer is B-cell lymphoma associated with low
levels of CD20 expression.
8. The method of claim 7, wherein the B-cell lymphoma is B-cell chronic lymphocytic
25 leukemia (B-CLL).
9. The method of claim 7, wherein the B-cell lymphoma is a marginal zone lymphoma.
10. The method of claim 1, wherein the anti-CD20 antibody is C2B8.
- 30 11. The method of claim 1, wherein the anti-CD20 antibody is Rituximab.

12. The method of claim 1, wherein the nucleic acid does not hybridize with genomic DNA or RNA under stringent conditions.

13. The method of claim 1, wherein the nucleic acid has a modified backbone.

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14. The method of claim 13, wherein the modified backbone is a phosphate backbone modification.

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15. The method of claim 13, wherein the modified backbone is a peptide modified oligonucleotide backbone.

16. The method of claim 1, wherein the nucleic acid is an immunostimulatory nucleic acid.

17. The method of claim 1, wherein the nucleic acid is 8 to 40 nucleotides in length.

18. The method of claim 1, wherein the nucleic acid is isolated.

19. The method of claim 1, wherein the nucleic acid is a synthetic nucleic acid.

20. The method of claim 1, wherein the nucleic acid and the anti-CD20 antibody are administered together.

21. The method of claim 1, wherein the nucleic acid and the anti-CD20 antibody are administered separately.

22. A method for diagnosing lymphoma, comprising:

isolating a B cell from a subject having or suspected of having a type of lymphoma and identifying a change in a cell surface marker when the B cell is contacted with an immunostimulatory nucleic acid, wherein the cell surface marker induced on the B cell is indicative of the type of lymphoma.

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23. The method of claim 22, further comprising a method for treating cancer by administering to the subject an immunostimulatory nucleic acid and an antibody specific for the cell surface marker induced on the B cell in order to treat the cancer.

5 24. A method for treating or preventing cancer, comprising:
administering to a subject having or at risk of developing cancer an effective amount to induce expression of a surface antigen on a cancer cell surface, of a nucleic acid, and
administering to the subject an antibody selected from the group consisting of an anti-CD22 antibody and an anti-CD19 antibody.

10 25. The method of claim 24, wherein the nucleic acid is an immunostimulatory CpG nucleic acid having an unmethylated CpG motif.

15 26. The method of claim 24, wherein the nucleic acid is an immunostimulatory T-rich nucleic acid.

20 27. The method of claim 24, wherein the nucleic acid is an immunostimulatory poly-G nucleic acid.

25 28. The method of claim 24, wherein the nucleic acid is bacterial DNA.

29. The method of claim 24, wherein the nucleic acid is eukaryotic DNA.

30 30. The method of claim 24, wherein the anti-CD22 antibody is a human IgG1 antibody.

31. The method of claim 24, wherein the anti-CD22 antibody is a murine IgG2a antibody.

32. The method of claim 24, wherein the anti-CD19 antibody is a human IgG1 antibody.

30 33. The method of claim 24, wherein the anti-CD19 antibody is a murine IgG2a antibody.

34. A method for treating lymphoma, comprising:

isolating a B cell from a subject having lymphoma,
identifying a surface antigen which is not expressed or which is expressed on the
surface of the B cell in an amount lower than that of a control B cell,
administering to the subject an antibody specific for the identified surface antigen and
an immunostimulatory nucleic acid in order to treat the cancer, wherein the
immunostimulatory nucleic acid is administered in an effective amount to upregulate
expression of the surface antigen on the cancer cell surface.

35. The method of claim 34, wherein the surface antigen is CD20.

36. The method of claim 34, wherein the surface antigen is CD40.

37. The method of claim 34, wherein surface antigen is CD22.

38. The method of claim 34, wherein surface antigen is CD19.

39. The method of claim 34, wherein the lymphoma is B-CLL.

40. The method of claim 34, wherein the lymphoma is marginal zone lymphoma.

41. The method of claim 34, wherein the antibody is a human IgG1 antibody.

42. The method of claim 34, wherein the antibody is a murine IgG2a antibody.

43. A method for treating a lymphoma resistant to antibody therapy, comprising:
administering to a subject having a lymphoma resistant to therapy with an antibody
specific for a surface antigen, an antibody specific for the surface antigen to which the
lymphoma is resistant and a nucleic acid in order to treat the lymphoma, wherein the nucleic
acid is administered in an effective amount to upregulate expression of the surface antigen on
the lymphoma cell surface.

44. The method of claim 43, wherein the surface antigen is CD20.

45. The method of claim 44, wherein the antibody is Rituximab.
46. The method of claim 43, wherein the surface antigen is CD40.
47. The method of claim 43, wherein the surface antigen is CD22.
48. The method of claim 43, wherein the surface antigen is CD19.
49. The method of claim 43, wherein the antibody is a human IgG1 antibody.
50. The method of claim 43, wherein the antibody is a murine IgG2a antibody.
51. The method of claim 43, further comprising administering an anti-cancer therapy.
52. The method of claim 51, wherein the anti-cancer therapy is selected from the group consisting of a chemotherapeutic agent or a cancer vaccine.
53. The method of claim 52, wherein the chemotherapeutic agent is selected from the group consisting of methotrexate, vincristine, adriamycin, cisplatin, mitomycin C, bleomycin, doxorubicin, dacarbazine, taxol, valrubicin, Novantrone/Mitroxantrone, Evacet/liposomal doxorubicin, Yewtaxan/Paclitaxel, Taxol/Paclitaxel, Furtulon/Doxifluridine, Cyclopax/oral paclitaxel, SPU-077/Cisplatin, HMR 1275/Flavopiridol, BMS-182751/oral platinum, Leustatin/Cladribine, Paxex/Paclitaxel, Doxil/liposomal doxorubicin, Caelyx/liposomal doxorubicin, Fludara/Fludarabine, Pharmarubicin/Epirubicin, DepoCyt, Caetyx/liposomal doxorubicin, Gemzar/Gemcitabine, Ifes/Mesnex/Ifosamide, Vumon/Teniposide, Paraplatin/Carboplatin, Plantinol/cisplatin, Vepeside/Etoposide, Taxotere/Docetaxel, prodrug of guanine arabinoside, nitrosoureas, Asparaginase, Busulfan, Carboplatin, Chlorombucil, Cytarabine HCl, Daunorubicin HCl, Etoposide (VP16-213), Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alfa-2a, Interferon Alfa-2b, Lomustine (CCNU), Mechlorethamine HCl (nitrogen mustard), Mercaptopurine, Mesna, Mitoxantrone HCl,

Procarbazine HCl, Thioguanine, Thiotepa, Vinblastine sulfate, Azacitidine, Interleukin 2, Pentostatin (2'deoxycoformycin), Teniposide (VM-26), GM-CSF, and Vindesine sulfate.

54. The method of claim 52, wherein the chemotherapeutic agent is selected from the group consisting of methotrexate, vincristine, adriamycin, cisplatin, mitomycin C, bleomycin, doxorubicin, dacarbazine, taxol, valrubicin, Novantrone/Mitroxantrone, Evacet/liposomal doxorubicin, Yewtaxan/Paclitaxel, Taxol/Paclitaxel, SPU-077/Cisplatin, HMR 1275/Flavopiridol, BMS-182751/oral platinum, Leustatin/Cladribine, Paxex/Paclitaxel, Doxil/liposomal doxorubicin, Caelyx/liposomal doxorubicin, Fludara/Fludarabine, Pharmarubicin/Epirubicin, DepoCyt, Caetyx/liposomal doxorubicin, Gemzar/Gemcitabine, Ifes/Mesnex/Ifosamide, Vumon/Teniposide, Paraplatin/Carboplatin, Plantinol/cisplatin, Vepeside/Etoposide, Taxotere/Docetaxel, prodrug of guanine arabinoside, nitrosoureas, alkylating agents such as melphalan and cyclophosphamide, Asparaginase, Busulfan, Carboplatin, Chlorombucil, Cytarabine HCl, Daunorubicin HCl, Etoposide (VP16-213), Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alfa-2a, Interferon Alfa-2b, Lomustine (CCNU), Mechlorethamine HCl (nitrogen mustard), Mercaptopurine, Mitoxantrone HCl, Procarbazine HCl, Thioguanine, Thiotepa, Vinblastine sulfate, Azacitidine, Interleukin 2, Pentostatin (2'deoxycoformycin), Teniposide (VM-26), GM-CSF, and Vindesine sulfate.

55. The method of claim 52, wherein the cancer vaccine is selected from the group consisting of EGF, Anti-idiotypic cancer vaccines, Gp75 antigen, GMK melanoma vaccine, MGv ganglioside conjugate vaccine, Her2/neu, Ovarex, M-Vax, O-Vax, L-Vax, STn-KHL theratope, BLP25 (MUC-1), liposomal idiotype vaccine, Melacine, peptide antigen vaccines, toxin/antigen vaccines, MVA-based vaccine, PACIS, BCG vaccine, TA-HPV, TA-CIN, DISC-virus and ImmuCyst/TheraCys.

56. A method for treating cancer in a human, comprising:
administering to a human an immunostimulatory nucleic acid and an antibody of IgG1 isotype, which binds to a cell surface antigen of a cancer cell and wherein the nucleic acid and the antibody are administered in an effective amount for killing the cancer cell.

57. The method of claim 56, wherein the nucleic acid is an immunostimulatory CpG nucleic acid having an unmethylated CpG motif.

58. The method of claim 56, wherein the nucleic acid is an immunostimulatory T-rich nucleic acid.

59. The method of claim 56, wherein the nucleic acid is an immunostimulatory poly-G nucleic acid.

60. The method of claim 56, wherein the nucleic acid is bacterial DNA.

61. The method of claim 56, wherein the nucleic acid is eukaryotic DNA.

62. The method of claim 56, wherein the nucleic acid has a modified backbone.

63. The method of claim 62, wherein the modified backbone is a phosphate backbone modification.

64. The method of claim 62, wherein the modified backbone is a peptide modified oligonucleotide backbone.

65. The method of claim 56, wherein the nucleic acid is an immunostimulatory nucleic acid.

66. The method of claim 56, wherein the nucleic acid is 8 to 40 nucleotides in length.

67. The method of claim 56, wherein the nucleic acid is isolated.

68. The method of claim 56, wherein the nucleic acid is a synthetic nucleic acid.

69. The method of claim 56, wherein the nucleic acid and the antibody are administered together.

70. The method of claim 56, wherein the nucleic acid and the antibody are administered separately.

71. The method of claim 56, further comprising administering an anti-cancer therapy.

72. The method of claim 71, wherein the anti-cancer therapy is selected from the group consisting of a chemotherapeutic agent and a cancer vaccine.

73. The method of claim 72, wherein the chemotherapeutic agent is selected from the group consisting of methotrexate, vincristine, adriamycin, cisplatin, non-sugar containing chloroethylnitrosoureas, 5-fluorouracil, mitomycin C, bleomycin, doxorubicin, dacarbazine, taxol, fragyline, Meglamine GLA, valrubicin, carmustaine and poliferposan, MMI270, BAY 12-9566, RAS famesyl transferase inhibitor, famesyl transferase inhibitor, MMP, MTA/LY231514, LY264618/Lometexol, Glamolec, CI-994, TNP-470, Hycamtin/Topotecan, PKC412, Valspodar/PSC833, Novantrone/Mitroxantrone, Metaret/Suramin, Batimastat, E7070, BCH-4556, CS-682, 9-AC, AG3340, AG3433, Incel/VX-710, VX-853, ZD0101, ISI641, ODN 698, TA 2516/Marmistat, BB2516/Marmistat, CDP 845, D2163, PD183805, DX8951f, Lemonal DP 2202, FK 317, Picibanil/OK-432, AD 32/Valrubicin, Metastron/strontium derivative, Temodal/Temozolomide, Evacet/liposomal doxorubicin, Yewtaxan/Paclitaxel, Taxol/Paclitaxel, Xeload/Capecitabine, Furtulon/Doxifluridine, Cyclopax/oral paclitaxel, Oral Taxoid, SPU-077/Cisplatin, HMR 1275/Flavopiridol, CP-358 (774)/EGFR, CP-609 (754)/RAS oncogene inhibitor, BMS-182751/oral platinum, UFT(Tegafur/Uracil), Ergamisol/Levamisole, Eniluracil/776C85/5FU enhancer, Campto/Levamisole, Camptosar/Irinotecan, Tumodex/Ralitrexed, Leustatin/Cladribine, Paxex/Paclitaxel, Doxil/liposomal doxorubicin, Caelyx/liposomal doxorubicin, Fludara/Fludarabine, Pharmarubicin/Epirubicin, DepoCyt, ZD1839, LU 79553/Bis-Naphtalimide, LU 103793/Dolastain, Caetyx/liposomal doxorubicin, Gemzar/Gemcitabine, ZD 0473/Anormed, YM 116, Iodine seeds, CDK4 and CDK2 inhibitors, PARP inhibitors, D4809/Dexifosamide, Ifes/Mesnex/Ifosamide, Vumon/Teniposide, Paraplatin/Carboplatin, Plantinol/cisplatin, Vepeside/Etoposide, ZD 9331, Taxotere/Docetaxel, prodrug of guanine arabinoside, Taxane Analog, nitrosoureas, alkylating agents such as melphalan and

cyclophosphamide, Aminoglutethimide, Asparaginase, Busulfan, Carboplatin, Chlorombucil, Cytarabine HCl, Dactinomycin, Daunorubicin HCl, Estramustine phosphate sodium, Etoposide (VP16-213), Floxuridine, Fluorouracil (5-FU), Flutamide, Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alfa-2a, Interferon Alfa-2b, Leuprolide acetate (LHRH-releasing factor analogue), Lomustine (CCNU), Mechlorethamine HCl (nitrogen mustard), Mercaptopurine, Mesna, Mitotane (o,p'-DDD), Mitoxantrone HCl, Octreotide, Plicamycin, Procarbazine HCl, Streptozocin, Tamoxifen citrate, Thioguanine, Thiotepa, Vinblastine sulfate, Amsacrine (m-AMSA), Azacitidine, Erythropoietin, Hexamethylmelamine (HMM), Interleukin 2, Mitoguazone (methyl-GAG; methyl glyoxal bis-guanyldihydrazone; MGBG), Pentostatin (2'-deoxycoformycin), Semustine (methyl-CCNU), Teniposide (VM-26), GM-CSF, and Vindesine sulfate.

74. The method of claim 72, wherein the chemotherapeutic agent is selected from the group consisting of methotrexate, vincristine, adriamycin, cisplatin, mitomycin C, bleomycin, doxorubicin, dacarbazine, taxol, valrubicin, Novantrone/Mitroxantrone, Evacet/liposomal doxorubicin, Yewtaxan/Paclitaxel, Taxol/Paclitaxel, SPU-077/Cisplatin, HMR 1275/Flavopiridol, BMS-182751/oral platinum, Leustatin/Cladribine, Paxex/Paclitaxel, Doxil/liposomal doxorubicin, Caelyx/liposomal doxorubicin, Fludara/Fludarabine, Pharmarubicin/Epirubicin, DepoCyt, Caetyx/liposomal doxorubicin, Gemzar/Gemcitabine, Ifes/Mesnex/Ifosamide, Vumon/Teniposide, Paraplatin/Carboplatin, Plantinol/cisplatin, Vepeside/Etoposide, Taxotere/Docetaxel, prodrug of guanine arabinoside, nitrosoureas, alkylating agents such as melphalan and cyclophosphamide, Asparaginase, Busulfan, Carboplatin, Chlorombucil, Cytarabine HCl, Daunorubicin HCl, Etoposide (VP16-213), Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alfa-2a, Interferon Alfa-2b, Lomustine (CCNU), Mechlorethamine HCl (nitrogen mustard), Mercaptopurine, Mitoxantrone HCl, Procarbazine HCl, Thioguanine, Thiotepa, Vinblastine sulfate, Azacitidine, Interleukin 2, Pentostatin (2'-deoxycoformycin), Teniposide (VM-26), GM-CSF, and Vindesine sulfate.

75. The method of claim 72, wherein the cancer vaccine is selected from the group consisting of EGF, Anti-idiotypic cancer vaccines, Gp75 antigen, GMK melanoma vaccine, MGv ganglioside conjugate vaccine, Her2/neu, Ovarex, M-Vax, O-Vax, L-Vax, STn-KHL

theratope, BLP25 (MUC-1), liposomal idiotypic vaccine, Melacine, peptide antigen vaccines, toxin/antigen vaccines, MVA-based vaccine, PACIS, BCG vaccine, TA-HPV, TA-CIN, DISC-virus and ImmuCyst/TheraCys.

- 5 76. A kit, comprising:
a package including at least two containers,
the first container housing an immunostimulatory nucleic acid,
the second container housing an antibody specific for a cell surface antigen, and
instructions for screening a cell to determine whether the immunostimulatory nucleic acid
10 upregulates expression of the cell surface antigen.

77. The kit of claim 76, wherein the antibody is selected from the group consisting of an anti-CD20 antibody, an anti-CD19 antibody, and an anti-CD22 antibody.

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